

In Brief

Classifications in Brief

Enneking Classification: Benign and Malignant Tumors of the Musculoskeletal System

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History

Since its establishment in 1959, the American Joint Committee for Cancer (AJCC) has undertaken the responsibility for developing clinically useful staging systems for various types of cancer. The task force on malignant bone tumors of the AJCC could not agree on a satisfactory system and recommended institutions with access to large numbers of patients, consistency in management, and long-term followups undertake this task [2]. In 1980, a system for surgical staging of musculoskeletal sarcoma was proposed, studied, and adopted by the Musculoskeletal Tumor Society and subsequently by the AJCC [4]. This system was established initially at the University of Florida in 1977 based on the data collected from 1968 through 1976 by Dr. William Enneking.

Purpose

An ideal staging system should be practical, reproducible, and of prognostic significance. Cancer staging is deemed critical for disease control in an individual patient and for the population at large. As defined by the International Union Against Cancer, the objectives of cancer staging are (1) to aid in planning the course of treatment, (2) to provide

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insight into the prognosis, (3) to assist in evaluating the results of treatment, (4) to facilitate effective interinstitutional communication, and (5) to contribute to continuing investigation of human malignancies [7].

Historically, surgical resection has been the cornerstone for management of musculoskeletal sarcomas. Thus the most useful staging system would guide the nature of the surgical procedure. It also should (1) organize the most significant prognostic factors into a system describing progressive degrees of risk to which a patient is subjected, (2) outline progressive stages of the disease having specific implications for surgical management, and (3) provide guidelines for use of adjunctive therapy.

Enneking Staging System

There are separate staging systems for benign and malignant mesenchymal tumors. The staging system for benign musculoskeletal tumors (Table 1) consists of three categories: ie, latent, active, and aggressive [4]. The classification is based on radiographic characteristics of the tumor host margin. Well-demarcated borders are indicative of latent lesions whereas indistinct borders result from permeation into host bone and a more aggressive lesion [11]. For benign tumors, local aggressiveness and incidence of recurrence increase with increase in surgical grade. Metastases are rare for locally aggressive benign lesions but do rarely occur in giant cell tumor and chondroblastoma [8, 12].

The Enneking surgical staging system for malignant mesenchymal tumors takes into account the surgical grade (G, G1, G2), local extent (T, T1, T2), and presence or absence of metastasis (M0, M1) [4]. The staging system for malignant musculoskeletal sarcomas (Table 2) consists of

Table 1. Enneking staging for benign musculoskeletal tumors based on radiographic characteristics of the tumor host margin

Stage	Description
Latent	Well-demarcated borders
Active	Indistinct borders
Aggressive	Indistinct borders

three stages. Stage III represents any tumor with distant metastasis. Stages I and II are based on surgical grade of the tumor. Each stage is further divided into two subcategories (A, B) based on the local extent of tumor. The stage of the tumor dictates the extent of surgical resection and margin.

In the Enneking staging system, a neoplasm is classified as either low (G1) or high (G2) grade. A low-grade lesion corresponds to Broder's Grades 1 or 2 [4] with a low risk for distant spread (< 25%). These tumors are characterized by low mitotic rates, low nuclear to cytoplasmic ratio, and limited pleomorphism. However, high-grade lesions (Broder's Grades 3 and 4) have a higher incidence of metastasis and are characterized histologically by mitotic figures, prominent nucleoli, and pleomorphism. Each lesion ultimately is assessed on histologic features; however, some tumors are high grade by definition, such as a dedifferentiated chondrosarcoma [3].

In addition to the histologic features, the staging takes into account the clinical and radiographic features. This includes axial imaging to determine the anatomic confines of the primary tumor and the presence of metastasis. Local extent for any neoplasm refers to its containment in anatomic boundaries of a compartment. Anatomic compartments have inherent barriers to tumor spread, including fascial planes and bone structures. Thus local extent determines the approach for surgical procedure and feasibility for desired surgical margins. In general, a high-grade lesion is more likely to invade surrounding host tissue. This places the patient at greater risk of local recurrence and metastasis. The use of adjuvant therapies then is indicated to eradicate tumor cells that would remain after surgical resection.

Table 2. Enneking staging for malignant musculoskeletal tumors based on surgical grade, local extent, and presence or absence of metastasis

Stage	Grade	Site	Metastasis
IA	Low (G1)	Intracompartamental (T1)	No metastasis (M0)
IB	Low (G1)	Extracompartamental (T2)	No metastasis (M0)
IIA	High (G2)	Intracompartamental (T1)	No metastasis (M0)
IIB	High (G2)	Extracompartamental (T2)	No metastasis (M0)
III	Any (G)	Any (T)	Regional or distant metastasis (M1)

(Adapted and published with permission of Lippincott Williams & Wilkins from Enneking WF, Spanier SS, Goodman MA. A system for the surgical staging of musculoskeletal sarcoma. *Clin Orthop Relat Res.* 1980;153:106–120.)

Table 3. Description of the TGNM system of the American Joint Committee for Cancer for staging of soft tissue sarcomas

TGNM component	Description	
Primary tumor (T)		
TX	Primary tumor cannot be assessed	
T0	No evidence of primary tumor	
T1	Tumor ≤ 5 cm	
	T1a	Superficial tumor
	T1b	Deep tumor
T2	Tumor ≥ 5 cm	
	T2a	Superficial tumor
	T2b	Deep tumor
Regional lymph nodes (N)		
NX	Regional lymph nodes cannot be assessed	
N0	No regional node metastasis	
N1	Regional lymph node metastasis	
Distant metastasis (M)		
MX	Distant metastasis cannot be assessed	
M0	No distant metastasis	
M1	Distant metastasis	
Histologic grade (G)		
GX	Grade cannot be assessed	
G1	Well differentiated	
G2	Moderately differentiated	
G3	Poorly differentiated	
G4	Dedifferentiated or anaplastic	

(Adapted and published with permission of Wolters Kluwer Health from Mendenhall WM, Indelicato DJ, Scarborough MT, Zlotek RA, Gibbs CP, Mendenhall NP, Mendenhall CM, Enneking WF. The management of adult soft tissue sarcomas. *Am J Clin Oncol.* 2009;32:436–442.)

The AJCC has proposed their own staging system for soft tissue sarcomas in contrast to bone sarcomas [9]. The AJCC staging follows a TGNM system, in which T (tumor) refers to the size of the primary neoplasm with an arbitrary limit of 5 cm, further categorized as superficial or deep; G (grade) refers to the histopathologic grade; N (nodes) refers to the presence of lymph node involvement; and M (metastasis) refers to the distant spread to other organs (Table 3). Articulation with surgical procedure is limited

when compared with the Enneking staging system because of lack of consideration to anatomic planes and compartments.

Confirmation/Validation

The Enneking surgical staging has been validated in two distinct situations: (1) intramurally by the University of Florida musculoskeletal oncology service (258 patients) [5] and (2) extramurally by a multicentric study (13 institutions) conducted by the Musculoskeletal Tumor Society (139 patients) [5]. Difficulty in using the system was reported in 5.5% of the cases studied extramurally. Almost all the reported problems were related to assessing compartmental containment of tumor. The probability of survival as a function of stage for intracompartmental and extracompartmental groups was similar [5]. However, the probability of survival for the combined group of 397 patients was lower ($p < 0.01$) for each subsequent stage every year [5].

Limitations

The Enneking surgical staging system is based on the natural evolution of mesenchymal tumors and thus is not applicable to tumors originating in either the marrow or reticuloendothelial system. These include lymphomas, multiple myeloma, plasmacytoma, Ewing's sarcoma, other round cell neoplasms, and metastatic carcinomas. Lesions originating in the skull also behave differently and thus cannot be staged or classified using this system.

The size of the primary tumor has been implicated as an important prognostic factor for numerous soft tissue sarcomas [6]. Larger lesions may be more likely to metastasize and may benefit from adjuvant chemotherapy [10]. The Enneking surgical staging system does not consider this important factor. This parameter is accounted for in the AJCC staging system for soft tissue sarcomas, but this classification lacks consideration of anatomic boundaries. Ideally, a combination of the staging systems may provide a stronger instrument than either alone.

For spinal column tumors, the Enneking surgical staging system does not take into account the presence of a continuous epidural compartment, neurologic implication of sacrificing the spinal cords and roots, and need for restoring spinal stability. Use of this system along with the Weinstein-Boriani-Biagini (WBB) classification has been studied for spinal tumors and appears to be safe and feasible and to improve disease control and survival, although both systems show only moderate interobserver reliability and additional studies are warranted [1]. Classification is considered safe when prognostication outlined in the classification system corresponds and correlates with outcomes

in clinical practice. It can improve disease control by providing a systematic approach towards treatment decisions.

Conclusions/Uses

The Enneking surgical staging system is reliable, reproducible, and of prognostic importance for musculoskeletal sarcomas, especially for those originating in the axial skeleton. It has been used widely for classification by orthopaedic oncologic surgeons around the world. However, this classification system is applicable only to mesenchymal malignancies.

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